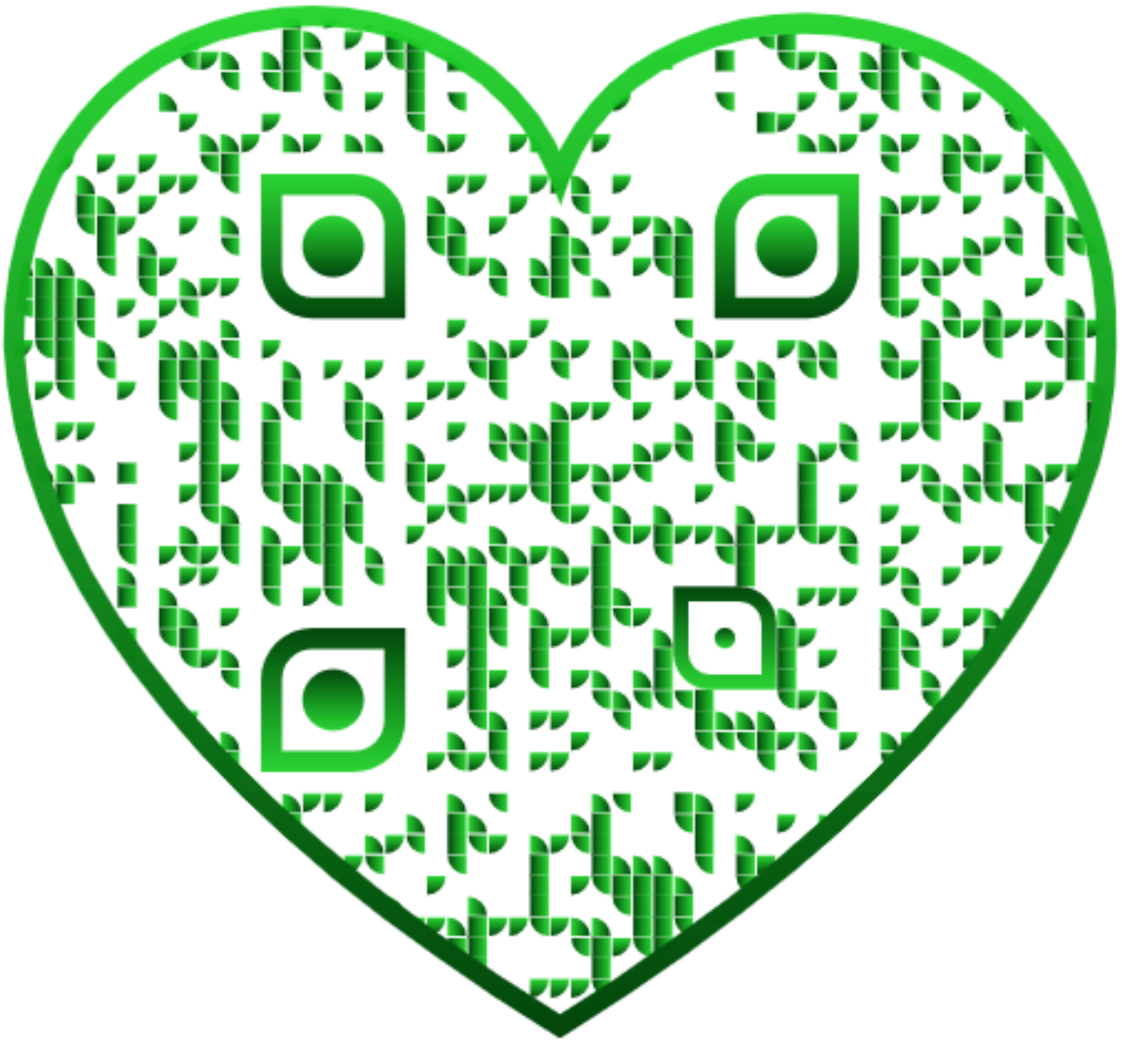
Drug eruptions



Drug eruptions

- Almost any drug can cause a cutaneous reaction
- Many inflammatory skin conditions can be caused or exacerbated by drugs

•NOTES:

_The very worst stage of drug eruption is Steven Jonson syndrome which is considered an emergency

_plaque psoriasis "chronic" is characterized by erythematous bleeding on the elbow or on the knee

_When using anti hypertension or anti malarial drugs it leads to pustule psoriasis which is considered as an emergency with a high mortality rate

Mechanisms

1. Non-allergic drug reactions

- result of overdosage, accumulation of drugs, unwanted pharmaco-logical effects, idiosyncratic, or a result of alterations of ecological balance
- They are a normal biological effect
- often predictable
- affect many, or even all, patients taking the drug at a sufficient dosage for a sufficient time

_Not related to immunity so it can affect any patient

_**Accumulation**: giving larg doses for a prolonged time

_Pharmaco_logical effect: always explain the side effects to the patient

Mechanisms

2. Allergic drug reactions

- less predictable.
- occur in only a minority of patients receiving a drug
- occur even with low doses
- They are not a normal biological effect of the drug and usually appear after the latent period required for induction of an immune response
- Chemically related drugs may cross-react
- majority of allergic drug reactions are caused by cell-mediated immune reaction

Some mechanisms involved in drug reactions

Table 25.1 Some mechanisms involved in drug reactions.

Pharmacological
Caused by overdosage or failure to excrete or metabolize
Cumulative effects
Altered skin ecology
Allergic
IgE-mediated
Cytotoxic
Immune complex-mediated
Cell-mediated
Idiosyncratic
Exacerbation of pre-existing skin conditions

Presentation

Antibiotics

Penicillins and sulphonamides

- are most commonly causing allergic reactions.
- These are often morbilliform but urticaria, erythema multiforme and fixed eruptions are common too.
- DDx. Is viral infections as often associated with exanthems
- Most patients with infectious mononucleosis develop a morbilliform rash if ampicillin is administered.
- Penicillin is a common cause of severe **anaphylactic reactions**, which can be life-threatening.

Minocycline

- can accumulate in the tissues and produce a brown or grey colour in the mucosa, sun-exposed areas or at sites of inflammation, as in the lesions of acne
- hepatitis, worsen lupus erythematosus or elicit a transient lupus-like syndrome

Fig. 25.2 Symmetrical erythematous maculopapular rash as a result of ampicillin.

Oral contraceptives

- Reactions to these are less common now that their hormonal content is small.

1. telogen effluvium
2. Melasma, hirsutism
3. erythema nodosum
4. acne
5. photosensitivity

Steroids

Cutaneous side-effects from systemic steroids include:

- a ruddy face
- cutaneous atrophy
- striae
- hirsutism
- an acneiform eruption
- a susceptibility to cutaneous infections, which may be atypical

Fig. 25.1 Gross striae caused by systemic steroids.

Anticonvulsants

Skin reactions to phenytoin, carbamazepine, lamotrigine and phenobarbital are common and include:

- erythematous, morbilliform, urticarial and purpuric rashes.
- rarely TEN, erythema multiforme, exfoliative dermatitis, DRESS syndrome and a lupus erythematosuslike syndrome

_**Dress syndrome**: It is a severe, idiosyncratic multisystem reaction to a drug, characterised by fever, skin rash, lymphadenopathy, haematological abnormalities and internal organ involvement.

Some common reaction patterns and drugs that can cause them

Toxic (reactive) erythema

- most common type of drug eruption
- looking like measles or scarlet fever, and sometimes showing prominent urticarial or erythema multiforme-like elements.
- Itching and fever may accompany the rash.
- Culprits include antibiotics (especially ampicillin), sulphonamides and related compounds (diuretics and hypoglycaemics) and barbiturates

Fig. 25.4 Toxic erythema with urticarial features.

Urticaria

- salicylates are the most common, often working non-immunologically as histamine releasers.
- Antibiotics
- Urticaria may be part of a severe and generalized reaction (anaphylaxis) that includes bronchospasm and collapse

***Erythema multiforme* and Stevens–Johnson syndrome**

- Sulphonamides, barbiturates, lamotrigine and phenylbutazone

Purpura

- Thiazides, sulphonamides, barbiturates and anticoagulants

Bullous eruptions

- also in Stevens–Johnson syndrome
- Vancomycin, lithium, diclofenac, captopril, furosemide and amiodarone are associated with development of linear IgA bullous disease

Fixed drug eruptions

- Round erythematous or purple, and sometimes bullous plaques recur at the same site each time the drug is taken
- Pigmentation persists between acute episodes.
- The glans penis seems to be a favoured site.
- The causes of fixed drug eruptions in any country follow the local patterns of drug usage
- **Paracetamol** is currently the most common offender in the UK
- **Trimethoprim-sulfa** leads the list in the USA
- NSAIDs (including aspirin), antibiotics, systemic antifungal agents and psychotropic drugs lie high on the list of other possible offenders.

•In Yemen, the most common drugs that cause drug eruption are:

1_ Netronidazole (flagyl)

2_ Codeine

3_ laxatives

Fig. 25.6 Fixed drug eruption – an unusually severe bullous reaction.

Acneiform eruptions

- Lithium, iodides, bromides
- oral contraceptives, androgens or glucocorticosteroids
- Antitub erculosis and anticonvulsant

Lichenoid eruptions

- These resemble lichen planus but mouth lesions are uncommon and scaling and eczematous elements may be seen.
- antimalarials, NSAIDs, gold, phenothiazines

Hair loss

- Retinoid
- cytotoxic agents
- oral contraceptive

Hypertrichosis

- dose-dependent effect of diazoxide, minoxidil and ciclosporin

Pigmentation

- Melosma in oral contraceptive plus sun exposure
- Large doses of phenothiazines impart a blue–grey colour to exposed areas
- clofazimine makes the skin red
- mepacrine turns the skin yellow
- minocycline turns areas of leg skin a curious greenish grey colour

Xerosis

- oral retinoids
- nicotinic acid
- lithium

•The most common drugs that cause pigmentation are:

1_ Anti malarial

2_ Anti epileptic

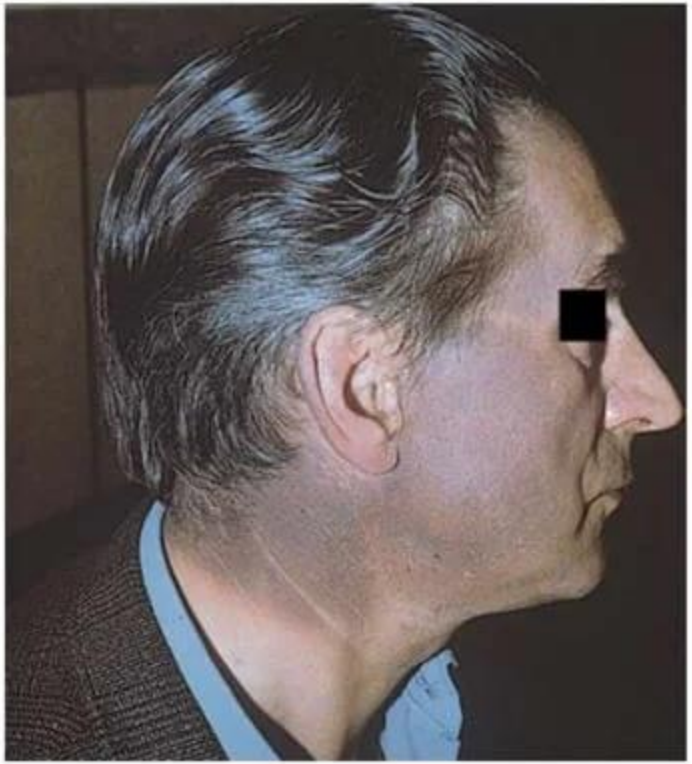


Fig. 25.8 Note sparing of skin creases and area shielded by spectacle frames in this patient with photorelated hyperpigmentation from a phenothiazine drug.

Course

- If an allergic reaction occurs during the first course of treatment, it characteristically begins late, often about the ninth day, or even after the drug has been stopped
- In previously exposed patients the common morbilliform allergic reaction starts 2–3 days after the administration of the drug
- The speed with which a drug eruption clears depends on the type of reaction and the rapidity with which the drug is eliminated

Differential diagnosis

- Ranges over the whole subject of dermatology
- The general rule is never to forget the possibility of a drug eruption when an atypical rash is seen. Six vital questions should be asked

The six vital questions to be asked when a drug eruption is suspected.

1. Can you exclude a simple dermatosis (e.g. scabies or psoriasis) and the known skin manifestations of an underlying disorder (e.g. systemic lupus erythematosus)?
2. Does the rash itself suggest a drug eruption (e.g. urticaria, erythema multiforme)?
3. Does a past history of drug reactions correlate with current prescriptions?
4. Was any drug introduced a few days or weeks before the eruption appeared?
5. Which of the current drugs most commonly cause drug eruptions (e.g. penicillins, sulphonamides, thiazides, allopurinol, phenylbutazone)?
6. Does the eruption fit with a well-recognized pattern caused by one of the current drugs (e.g. an acneiform rash from lithium)?

Treatment

- The first approach is to withdraw the suspected drug, accepting that several drugs may need to be stopped at the same time.
- The decision to stop or continue a drug depends upon:

1. the nature of the drug
2. the necessity of using the drug for treatment
3. the availability of chemically unrelated alternatives
4. the severity of the reaction, its potential reversibility
5. the probability that the drug is actually causing the reaction.

- Every effort must be made to correlate the onset of the rash with prescription records.
- Often, but not always, the **latest drug** to be introduced is the most likely culprit.
- **Prick tests** and *in vitro* tests for allergy are unreliable to
- **Re-administration**, as a diagnostic test, is usually unwise except when no suitable alternative drug exists

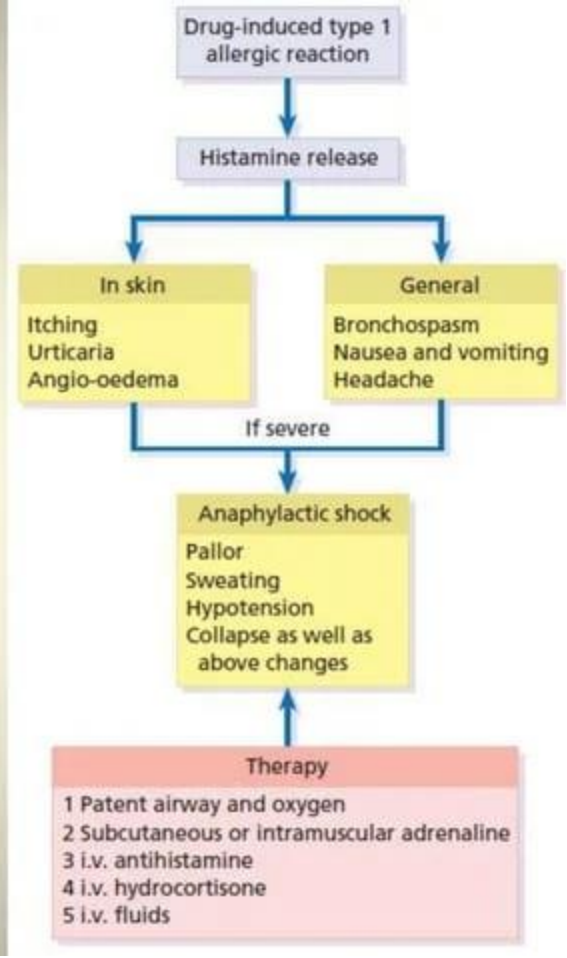
Non-specific therapy depends upon the type of eruption.

- In urticaria, antihistamines are helpful.
- In some reactions, topical or systemic corticosteroids can be used, and applications of calamine lotion may be soothing.
- Plasmapheresis and dialysis can be considered in certain life-threatening situations

Anaphylactic reactions

- ensure that the **airway** is not compromised (e.g. oxygen, assisted respiration or even emergency tracheostomy).
- **One or more injections of adrenaline** (epinephrine) (1 : 1000) 0.3–0.5 mL should be given subcutaneously or intramuscularly in adults
- slow (over 1 min) **intravenous injection of chlorphenamine maleate** (10–20 mg diluted in syringe with 5–10 mL blood).
- Although the action of intravenous **hydrocortisone** (100 mg) is delayed for several hours, it should be given to prevent further deterioration in severely affected patients.
- Patients should be observed for 6 h after their condition is stable, as late deterioration may occur.
- If an anaphylactic reaction is anticipated, patients should be taught how to self-inject adrenaline, and may be given a salbutamol inhaler to use at the first sign of the reaction

The cause, clinical features and treatment of anaphylaxis.



Desensitization

- is seldom advisable or practical
- **Mechanism**: making the immune system adapt by giving small sporadic doses in separated periods to the patient and increasing the dose slowly and gradually

- It's used when there are no other options

The End